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Statins and Vitamin D

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In the recent article by Pérez-Castrillón et al.[1], the authors found that atorvastatin therapy for 12 months significantly increased 25-hydroxyvitamin D (25-OHD) levels in patients with acute ischemic heart disease. We found a similar association between statin use and 25-OHD levels in a vitamin D3 supplementation trial that we conducted [2]. The design and primary results of the study have been published and summarized here. In brief, we conducted a 3-year randomized controlled trial to test the hypothesis that vitamin D3 supplementation would prevent bone loss in calcium-replete, African-American postmenopausal women. Participants received either 20 mcg/d (800 IU) of vitamin D3 or placebo. After 2 years, the vitamin D3 dose was increased to 50 mcg/d (2000 IU) in the active group. The study was approved by the Institutional Review Board of Winthrop-University Hospital.

A total of 208 women were randomized to receive vitamin D3 (n=104) or placebo (n=104). 51 women were on statins. At baseline, the subjects on statins had a significantly higher 25-OHD level than the subjects who were not on statins (51.2 ± 20.1 nmol/L versus 43.2 ± 18.0 nmol/L respectively, $p=0.008$). This was also true when averaging 25-OHD levels across the 3-year study period and looking at active and placebo patients separately. 185 subjects had follow-up 25-OHD levels drawn every 6 months during the study. Higher levels were seen in the statin use subgroup whether they were on placebo or active vitamin D (Figure 1). There was no interaction seen between vitamin D use and statin use, i.e. the impacts are additive ($p=0.5502$). This significant difference is comparable to the increase in 25-OHD levels seen in Pérez-Castrillón's study (41 ± 19 versus 47 ± 19 nmol/L, $p=0.003$) [1]. Although Pérez-Castrillón et al found a statistically significant relation between total cholesterol and 25-OHD ($r=0.277$, $p=0.002$), we did not find a significant relation between total cholesterol and 25-OHD in our study population.

A recent meta-analysis found that statin use was associated with fewer hip fractures (OR 0.60, 95% CI 0.45 – 0.78) and improved hip bone mineral density [3]. In-vitro studies reveal that statins induce osteoblast differentiation [4] and inhibit osteoclast formation [5], thus promoting bone formation. Perhaps one of the ways in which statins reduce fracture risk is by increasing 25-OHD levels. Few studies have looked at levels of vitamin D metabolites and statin use and they offer conflicting results [6-9]. There was concern when statins were first introduced that they would impair the formation of steroids dependent on the cholesterol synthetic pathway but it has been shown that vitamin D synthesis remains normal [10]. The mechanism by which statins increase vitamin D levels is not clear. Dedicated randomized controlled trials investigating statin therapy and vitamin D are needed.

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Statin	Active/Placebo	N	Mean 25-OHD (nmol/L)
No statin	Active	64	65.9 ± 20.6*
	Placebo	72	38.4 ± 12.8*
On statin	Active	29	74.0 ± 18.3*
	Placebo	20	50.0 ± 17.7*

* p = 0.0009 when comparing 25-OHD levels between no statin group and statin use group.

Figure 1.

Mean 25-hydroxyvitamin D levels by statin use and treatment group